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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,644	08/25/2008	Thomas Thisted	THISTED1A	4397

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EXAMINER	
GROSS, CHRISTOPHER M	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,644	THISTED ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-20,69-75 and 77-97* is/are pending in the application.

4a) Of the above claim(s) *69-75,77-82,85,86,89 and 93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18-20,83,84,87,88,90-92 and 94-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner charged with the present case has changed. See contact information below.

Responsive to communications entered 4/28/2010; 1/19/2011.

Claims 1-16,18-20, 69-75, 77-97 are pending.
Claims 69-75,77-82 and 85-86, 89, 93 are withdrawn.
Claims 1-16,18-20, 83,84, 87, 88, 90-92,94-97 are examined herein.

Priority

The present application was filed 8/25/2008 and is a 371 of PCT/DK2004/000630 filed 09/17/2004 and claims benefit of provisional applications 60504748 filed 09/22/2003 and 60509268 filed 10/08/2003.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to Danish applications PA2003 01356 filed 09/18/2003 and PA2003 01485 filed 10/08/2003. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Election/Restrictions

Upon further consideration the requirement for election of display molecule and its molecular weight, as set forth on p 2 item A of the restriction requirement mailed 7/21/2010 is hereby withdrawn.

Applicant's election with traverse of enzymatic ligation for the species of "relationship between target and identifier oligonucleotide" in the reply filed on 1/19/2011, reading on all claims except 85 and 86 according to applicant is

acknowledged. The traversal is on the ground(s) that that the generic claims are allowable. This is not found persuasive in view of the rejections set forth below.

Claims 85, 86 and dependent claims 89, 93 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/19/2011.

The requirement is still deemed proper and is therefore made FINAL.

Page 39 penultimate paragraphs of the 4/28/2010 response alleges the office action mailed 10/29/2009 was incomplete in so far as the (previous) examiner had not addressed the traversal in the 7/29/2009 election.

In this vein, the current examiner notes that no claims to the originally presented invention were withdrawn, thus while the office action mailed 10/29/2009 does not explicitly indicate so, the restriction mailed 2/4/2009 appears to have been withdrawn. In so far as any ambiguity remains: the restriction mailed 2/4/2009 is hereby **VACATED**, rendering applicants 7/29/2009 election with traverse moot.

Nevertheless, election of a particular target; and/or a member of bifunctional display molecule library specified as to atom and bond and/or election particular chemical entities for synthesis thereof *may* be required in the future in so far as applicant introduces future claims drawn to alternatives of a Markush-group that are of dissimilar nature in accordance with the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions.

From the penultimate paragraph on p 40 through the third paragraph on p 48 of the 4/28/2010 response, applicant alleges the withdrawal of claims 69-82 by original presentation in accordance with 37 CFR 1.142(b) and MPEP § 821.03 is improper based on 37 CFR 1.475(d) alone and similar claims "transferred" to related case 12095778 (referred to as '778) per the office action mailed 10/29/2009.

The examiner agrees that 37 CFR 1.475(d) alone and similar claims in related case 12095778 (referred to as '778) does not provide for basis for said withdrawal, however, as admitted in the last paragraph on p 40 4/28/2010, 37 CFR 1.475(a) certainly does, in stating: "...Where a group of inventions is claimed in an application, the **requirement of unity of invention shall be fulfilled only when there is** a technical relationship among those inventions involving one or more of the same or corresponding **special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."** Emphasis Added.

Here, unity of invention is lacking because even though the technical feature of 'generating a conjugate comprising a molecular target associated with a target oligonucleotide and a bifunctional complex comprising a display molecule attached to an identifier oligonucleotide which codes for said display molecule' is shared by the claims this technical feature is not a *special* technical feature, as it does not make a contribution over the prior art, in view of the 35 USC 102 (novelty) rejection and/or 35 USC 103 (inventive step) rejection(s) set forth below. Furthermore, the methods set

forth in claims 69-75,77-82 require materially different steps to perform (e.g. steps vi, vii of claim 69, 70 etc.).

The requirement is still deemed proper and is therefore made FINAL.

Specification

The amendment filed 4/28/2010 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The deleted material which must remain in the original disclosure is as follows: Page 10 of the 4/28/2010 amendment to the specification deletes p 112 lines 22-19 (or 119 ?), which discuss tetrazole activation and p 112 line 17, which discusses the means of repeating an oligonucleotide synthetic cycle. See also section (iv) below. Furthermore the brief description to figure 11 now includes a 5" nuclease, whereas on p 43 line 18 of the specification as filed concerned a 5' nuclease.

Applicant is required to cancel the new matter in the reply to this Office Action.

The disclosure is objected to because of the following informalities:

(i) In accordance with MPEP 601.01(g) if the drawings show Figures 1A, 1B, and 1C and the brief description of the drawings refers only to Figure 1, this is an error in the specification which must be corrected. Here, the brief description of figure 11 only refers to figure 11 rather than figures 11A and 11B.

(ii) By way of the instructions provided with the 4/28/2010 specification amendment on pp 2 and 10, the section entitled "Detailed Description of Figures 1-10"

is duplicated beginning on p 8, as is the Brief Description of the figures on now on p 8 and p 112 as previously presented.

(iii) Example 3 appears on pp 43-46 as opposed to following example 2 on p 126.

(iv) Applicant's 4/28/2010 amendment the destroys grammatical congruence in to second paragraph on p 112 of the specification making interpretation difficult.

Appropriate corrections are required.

Withdrawn Rejections and Objections

The objection to the specification under 37 C.F.R. § 1.77(b)(8), as raised in the last office action is hereby withdrawn in view of applicant's amendments thereto.

The rejection of claims 1-20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments.

The rejection of claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Szostak *et al.*, U.S. Patent No. 6,207,446, in view of Rabani *et al.*, U.S. Patent Appl. Publication No. 2004/0161741, published on August 19, 2004 is hereby withdrawn in view of applicant's amendments thereto.

New Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-16,18-20, 83,84,88, 95-97 are rejected under 35 U.S.C. 102(b) as being antipated by **Liu et al** (US Application Publication 2003/0113738).

The claimed subject matter is drawn to a method for identifying display molecule(s) having affinity towards molecular target(s), comprising the steps of:

providing one or more target complexes, each comprising a molecular target associated with a target oliqonucleotide,

providing a library of bifunctional complexes, each bifunctional complex of the library comprising a display molecule attached to an identifier oliqonucleotide that codes for said display molecule,

mixing said target complexes with said library of bifunctional complexes, so that said bifunctional complexes may bind to one or more of said target complexes, by virtue of interaction between the display molecule of said bifunctional complex and the target of said target complex,said couplinq being in addition to the indirect coupling., resulting from said binding of the display molecule to the target, and

deducing the identity of the binding display molecule(s) and/or the molecular target(s) from the coupled product between the identifier oligonucleotide(s) and the target

Liu et al teach, throughout the document and especially the abstract as well as paragraph 0111+, a method for synthesizing molecule libraries with a nucleic acid template.

In figure 9, Liu et al (top strand) teach providing a target complexes, each comprising a molecular target associated with a target oliqonucleotide (top strand); providing a library of bifunctional complexes (bottom strand(s) with 4 or more codons),

each bifunctional complex of the library comprising a display molecule attached to an identifier oliqonucleotide that codes for said display molecule; mixing said target complexes with said library of bifunctional complexes, so that said bifunctional complexes may covalently bind to one or more of said target complexes, by virtue of nucleophilic-electophilic interaction between the display molecule of said bifunctional complex and the target of said target complex, said couplinq being in addition to the indirect coupling. resulting from said binding of the display molecule to the target; and deducing the identity of the binding display molecule(s) and/or the molecular target(s) from the coupled product between the identifier oligonucleotide(s) and the target by gel electrophoresis, therein reading on claims 1,2 (codon part), 3, 6, 10, 12, 13, 88

In accordance with paragraph 0140 of Liu, the maleimide function for the reaction illustrated in figure 9 is connected through a 5' amino link structural unit incorporated during nascent oligonucleotide synthesis thus is a reaction product of two chemical entities which are not alpha amino acids nor is an alpha peptide, nor nucleic acid, is less than 500 Dalton per claims 2, 4, 5, 7, 8, 9, 11 83, 84

Figure 9 and 45 of Liu et al includes a backbone sequences which are taken as a framing sequence per claim 14.

Unlike the oligonucleotide phosphodiester backbone, the amide bond shown in figure 9 of Liu et al is selectively cleavable by reagents such as hydroxide, reading on claim 15.

In paragraph 0177, Liu et al suggest the method may be used to write a new genetic code for preparing chelating materials which release Nickel upon photolysis, reading on claim 16.

In paragraph 0112, Liu et al envision libraries with 1,000,000 members, as set forth in claim 18.

In paragraph 0098 and figure 11A and elsewhere, Liu et al describe anticodons bearing biotin targets (i.e. of biological origin), reading on claim 19.

Figure 26 of and paragraph 0175 Liu et al discloses solid supports, reading on claim 20.

In figure 12A, Liu et al teach amplification with PCR primers, reading on claims 95, 96,97 and 98.

Thus, the claims are anticipated.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16,18-20, 83,84,88, 95-97 and 87, 90, 91, 92, 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Liu et al** (US Application Publication 2003/0113738) in view of **Pedersen** (US Application Publication 2006/012170) as evidenced by Barany (1991 PNAS 88:189-193).

Liu et al is relied on as above.

Liu et al do not teach: enzymatic means to ligate the target oligonucleotide and the display oligonucleotide covalently, such as set forth in claims 87, 90, 91; a connector oligonucleotide, as set forth in claim 92; an identifier oligonucleotide with sticky ends, as set forth in claim 94.

Pedersen teaches, throughout the document and especially figure 19 and paragraph 0053, using a ligase (elected species) to ligate target and display oligonucleotides together forming a natural phosphodiester bond, therein reading on claims 87, 90, 91. In paragraph 0057, Pedersen teaches said ligase may employ a hair pin loop, which is fairly taken as type of sticky end per claim 94. In paragraph 0163, Pedersen et al suggest an alternative embodiment using the Ligase Chain Reaction (LCR), reading on claim 92, as LCR, invented by Barany, employs a connector oligonucleotide such as shown in figure 1 therein.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use hairpins and/or LCR in the manner of Pedersen with the library of Liu et al.

One of ordinary skill in the art would have been motivated to hairpins and /or LCR in the manner of Pedersen with the library of Liu et a because it would simplify deconvolution, since both the display molecule and target oligonucleotide could be decoded simultaneously in one sequencing run: In accordance with MPEP 2141 section III (A) citing *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 398, 82 USPQ2d 1385,1395 (2007), Combining prior art elements (oligonucleotide directed synthesis) according to known methods (LCR) to yield predictable results is obvious.

One of ordinary skill in the art would have had a reasonable expectation of success in applying LCR and/or hairpins per Pedersen toward library synthesis in the manner of Liu et al because each reference concerns nucleic acid directed synthesis, which has the advantage of high local concentration of reagents (see the abstract or each reference). Accordingly the teachings of Pedersen concerning LCR and hairpins fall squarely in the scope of technology of interest to Liu et al.

In conclusion, the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and was as a whole, *prima facie* obvious.

New Claim Rejections - 35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 1-16,18-20, 83, 84, 87, 88, 90-92, 94-97 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The antecedent basis for and/or the mixing step of claims line 10 recites vague and indefinite language in "said target complexes in" because the providing step (line 4) is for one or more. In particular it is not clear if there is a single target complex or multiple.

In accordance with MPEP 2173.02: If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See Morton Int 'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

As currently written, the metes and bounds of the claims are unascertainable. Therefore, claim 1 and all dependent claims are rejected under 35 USC 112, second paragraph.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571 272 0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,

/CHRISTOPHER M GROSS/
Primary Examiner, Art Unit 1639

CHRISTOPHER M GROSS
Primary Examiner
Art Unit 1639